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(71) Applicant (for all designated States except US): ISIS IN-  
NOVATION LIMITED [GB/GB]; Ewert House, Ewert  
Place, Summertown, Oxford OX2 7SG (GB).

(72) Inventor; and

(75) Inventor/Applicant (for US only): DAVIS, Simon  
[AU/GB]; Nuffield Department of Medicine, University  
of Oxford, Oxford OX3 9DU (GB).

(74) Agents: ROQUES, Sarah, Elizabeth et al; J.A. Kemp &  
Co., 14 South Square, Gray's Inn, London WC1R 5JJ (GB).

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(54) Title: MODULATORS OF CELL-SURFACE RECEPTORS OF THE IG-CLASS

(57) Abstract: Method of identifying a modulator of CD28 comprising comparing a structural model of a candidate modulator with a structural model of CD28 to thereby determine whether the modulator will bind to CD28, wherein the structural model is derived from, or comprises, structural coordinates of a crystal of: (i) CD28, (ii) a fragment of CD28, or (iii) a homologue of (i) or (ii). The crystal of CD28 in a soluble form complexed with the Fab fragment of a mitogenic (superagonistic) antibody has been obtained and used for the determination of the 3D-structure of the receptor. The application also relates to modulators of superagonistic signalling for any receptor of the CD28 family, i.e. to superagonistic antibodies and chimeric proteins thereof, and to the screening of the superagonistic modulators. In the methods of screening, the binding of the candidate modulators to a portion of the receptor proximal to the cell membrane is investigated.